Global Regulatory Policy

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July 8, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: Docket No. 2004N-0133 Electronic Record; Electronic Signatures; Public Meeting and Request for Comments

Merck & Co., Inc. is a leading worldwide human health product company. Merck Research Laboratories (MRL), a division of Merck & Co., Inc, is one of the leading U.S. biomedical research organizations.

We are providing comments and recommendations to the Food and Drug Administration (FDA) regarding implementation of Part 11, specifically, to the questions included in FDA's Notice of Public Meeting, issued April 8, 2004 (69 FR 18591).

General Comments

We have three general recommendations regarding the implementation of Part 11. First, we recommend that FDA incorporate a risk-based approach with regard to Part 11 implementation in line with the recent FDA guidance documents on this subject. A risk-based approach will, among other things, assist both the FDA and regulated industry in determining what records to archive and for how long, ensuring that industry meets predicate rule expectations. Our second recommendation is that FDA's implementation of Part 11 should not include legacy systems (i.e., systems installed and operational prior to the final rule). We believe the predicate rules currently in place for legacy systems are sufficient and should not fall under the purview of Part 11. Lastly, we believe FDA should define the term "record" more narrowly to only include the final electronic record, rather than every record from the first save of the electronic document through all intermediate analyses and quality control steps to the final document. If the current language, which includes all initial and intermediate records, is included in a regulation, we believe it will be overly burdensome to the drug development and manufacturing process.

Specific Comments

The enclosed table provides comments only for those questions posed by FDA in its above-referenced notice for which we have specific recommendations and explanations for those recommendations.

We appreciate the opportunity to share our comments and recommendations with FDA regarding this important issue. If we can provide further assistance, please do not hesitate to contact Christopher Bean, Director, Systems Services, at 215-652-6872 or Brian Mayhew, Regulatory Policy Analyst, at 301-941-1402.

Sincerely,

Lauren M. Hetrick

for Donald Black, MD, MBA
Vice President
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Enclosure

Section Paragraph	Proposed Change	Comment/ Rationale
IV. A. Subpart A – General Provisions, 1	Please incorporate into the Part 11 rule, the narrow interpretation of scope and the definition of Part 11 records, sections III., B.,1. and III.,B., 2., respectively from the Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application, August 2003. Perhaps the scope can be further modified to allow a risk analysis to justify which records are subject to Part 11. We further recommend that the scope of Part 11 exclude electronic documents from the requirements in 11.10(a), (c) through (h), and (k) and the corresponding requirements of 11.30.	The scope of Part 11 has been interpreted to be very broad and overly inclusive. The rule was seen as covering all electronic records from the very first save, through all intermediate analyses and quality control steps to the final document. This is seen as adding a very large burden to the drug development and manufacturing process. In addition to the narrower definition of Part 11 records that was stated in the Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application, there should be an opportunity to decide, via a risk analysis, when in the life of a record application of Part 11 is appropriate. We are aware that the histopathology notes are the only exception at this time. Early data that are used neither to make decisions about the compound nor used to support efficacy, safety or quality claims should be excluded from Part 11. We want the ability to define the point at which Part 11 controls must be applied. We would like there to be more flexibility in identifying a Part 11 record, for example when double keying for manual data entry is performed. If exceptions can be justified, they should be acceptable. The rationale for this exemption is delineated in FDAs 'Requirements for Submission of Labeling for Human Prescription Drugs and Biologics in Electronic Format' (21 CFR Parts 314 and 601), which explicitly exempts electronic labeling submissions from these Part 11 requirements. The FDA's rationale for the exemption is sound and should be extended to all documents that are reviewed prior to acting on or being submitting to FDA.
IV. B Subpart B – Electronic Records, 1	Please incorporate into the Part 11 rule, the concept of a justified and documented risk-based approach for the four areas (validation, audit trail, record retention and record copying) that is included in the Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application.	As the FDA moves forward, it should clarify that the risk-based approach applies to all activities subject to Part 11. A risk-based approach may acknowledge that some records have decreasing value over time. This will assist both the FDA and regulated industry in determining what records need to be archived and for how long.

Section Paragraph	Proposed Change	Comment/ Rationale
IV. B Subpart B – Electronic Records, 3	We think the scope for records submitted to FDA is different from that for electronic records maintained to satisfy predicate rule requirements. However, the requirements are the same for both record types.	There is no need for additional controls or clarity. The standards should be the same for both record types since the importance and integrity needs are the same. Many times the same records are used in both ways – submitted to FDA and retained to meet predicate rule requirements.
IV. B Subpart B – Electronic Records, 4	No changes are needed.	The additional measures required for open systems such as document encryption and appropriate digital signature standards to ensure record authenticity, integrity and confidentiality are appropriate.
IV. B Subpart B – Electronic Records, individual controls, 1	Please incorporate into the Part 11 rule, the concept of a justified and documented risk-based approach for the four areas (validation, audit trail, record retention and record copying) that is included in the Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application.	As the FDA moves forward, it should endorse the risk-based approach that is included in the Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application.
IV. D Subpart D – Additional questions, 3		There is a possibility that the requirements in Part 11 with discourage innovation where new software and hardware technology vendors have not implemented the technological controls that are expected to be provided by the vendor, e.g., security model and audit trails. Many hardware and software vendors are developing innovative systems for a much wider client base than just those industries regulated under the Federal Food, Drug and Cosmetic Act and the Public Health Service Act. These vendors may not include in their systems the necessary technological controls required by Part 11. Often, these new systems have immediate applicability in regulated industries but purchase and implementation must be deferred until the vendors implement the necessary technological controls.

Section Paragraph	Proposed Change	
IV. D Subpart D – Additional questions, 5	Please incorporate into the Part 11 rule for all required technological controls, the concept of a justified and documented risk-based approaches included in the Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application. We recommend that signatures that are not required by FDA predicate rules, but are required for business approvals or verifications, not be held to Part 11 signature requirements even when applied to Part 11 required records. We recommend that section 11.200(a) 3, be changed to state: 'Be administered and executed to ensure that attempted use of an individual's electronic signature by anyone other than its genuine owner cannot be accomplished by ordinary means.'	
IV. D Subpart D – Additional questions, 6	Please consider incorporating into the Part 11 rule, the concept of risk mitigation and appropriate controls included in the Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application, to eliminate concerns regarding application of Part 11 requirements to legacy systems.	Te predicate rule controls that were in place for legacy systems should be adequate.
IV. D Subpart D – Additional questions, 7	Please consider incorporating into the Part 11 rule, the concepts of using common portable formats and automated conversion or export methods to make copies in a more common format as stated in the Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application.	Conversion to technology neutral formats based on open standards will be very helpful in the preservation of trustworthy electronic records.